Listing of Claims

1. (currently amended) ~~An~~ The herpes simplex virus according to claim 94, wherein ~~the herpes simplex virus genome comprises~~ the nucleic acid ~~encoding~~ encodes an antisense to the squamous cell carcinoma related oncogene (asSCCRO).

2. (previously presented) The herpes simplex virus according to claim 1 wherein said nucleic acid encodes a mammalian asSCCRO.

3. (previously presented) The herpes simplex virus according to claim 1 wherein said nucleic acid encodes the human asSCCRO.

4. (previously presented) The herpes simplex virus according to claim 1 wherein said nucleic acid encodes a nucleotide sequence having at least 60% sequence identity to the nucleotide sequence complementary to:

(i) the polynucleotide sequence of SEQ ID No. 1 or 3 or its complement;

(ii) the mRNA transcript of SEQ ID No. 1 or 3; or

(iii) to a fragment of said polynucleotide sequence or mRNA transcript.

5. (previously presented) The herpes simplex virus according to claim 4 wherein said nucleic acid encodes a nucleotide sequence complementary to:

(i) the polynucleotide sequence of SEQ ID No. 1 or 3 or its complement;

(ii) the mRNA transcript of SEQ ID No. 1 or 3; or

(iii) to a fragment of said polynucleotide sequence or mRNA transcript.

6. (previously presented) The herpes simplex virus according to claim 4 wherein said degree of sequence identity is at least 70%.

7. (previously presented) The herpes simplex virus of claim 4 wherein a said fragment comprises at least 20 nucleotides and no more than 900 nucleotides.

8. (previously presented) The herpes simplex virus according to claim 1 wherein said nucleic acid hybridises under high stringency conditions to:

(i) the polynucleotide sequence of SEQ ID No. 1 or 3 or its complement;

(ii) the mRNA transcript of SEQ ID No. 1 or 3; or

(iii) a fragment of said polynucleotide sequence or mRNA transcript.

9. (previously presented) The herpes simplex virus of claim 1 wherein said herpes simplex virus genome further comprises a regulatory sequence operably linked to said nucleic acid encoding an antisense to the squamous cell carcinoma related oncogene (as SCCRO), wherein said regulatory sequence has a role in controlling transcription of said asSCCRO.

10. (previously presented) The herpes simplex virus of claim 1 wherein said nucleic acid is located in at least one RL1 locus of the herpes simplex virus genome.

11. (previously presented) The herpes simplex virus of claim 1 wherein said nucleic acid is located in, or overlaps, at least one of the ICP34.5 protein coding sequences of the herpes simplex virus genome.

12. (previously presented) The herpes simplex virus of claim 1 wherein the herpes simplex virus is a mutant of one of HSV-1 strains 17 or F or HSV-2 strain HG52.

13. (previously presented) The herpes simplex virus of claim 1 wherein the herpes simplex virus is a mutant of HSV-1 strain 17 mutant 1716.

14. (previously presented) The herpes simplex virus of claim 1 which is a gene specific null mutant.

15. (previously presented) The herpes simplex virus of claim 1 which is an ICP34.5 null mutant.

16. (previously presented) The herpes simplex virus of claim 1 which lacks at least one expressible ICP34.5 gene.

17. (previously presented) The herpes simplex virus of claim 1 which lacks only one expressible ICP34.5 gene.

18. (previously presented) The herpes simplex virus of claim 1 which is non-neurovirulent.

19. (previously presented) The herpes simplex virus of claim 1 wherein said nucleic acid encoding the asSCCRO forms part of a nucleic acid cassette integrated in the genome of said herpes simplex virus, said cassette comprising nucleic acid encoding:

(a) said asSCCRO; and nucleic acid encoding:

(b) a ribosome binding site; and

(c) a marker,

wherein the nucleic acid encoding asSCCRO is arranged upstream (5′) of the ribosome binding site and the ribosome binding site is arranged upstream (5′) of the marker.

20. (previously presented) The herpes simplex virus according to claim 19 wherein a regulatory nucleotide sequence is located upstream (5′) of the nucleic acid encoding asSCCRO, wherein the regulatory nucleotide sequence has a role in regulating transcription of said nucleic acid encoding the asSCCRO.

21. (previously presented) The herpes simplex virus as claimed in claim 19 wherein the cassette disrupts a protein coding sequence resulting in inactivation of the respective gene product.

22. (previously presented) The herpes simplex virus of claim 19 wherein a transcription product of the cassette is a bi- or poly- cistronic transcript comprising a first cistron encoding the asSCCRO and a second cistron encoding the marker nucleic acid wherein the ribosome binding site is located between said first and second cistrons.

23. (previously presented) The herpes simplex virus of claim 19 wherein the ribosome binding site comprises an internal ribosome entry site (IRES).

24. (previously presented) The herpes simplex virus of claim 19 wherein the marker is a defined nucleotide sequence encoding a polypeptide.

25. (previously presented) The herpes simplex virus as claimed in claim 24 wherein the marker comprises the Green Fluorescent Protein (GFP) protein coding sequence or the enhanced Green Fluorescent Protein (EGFP) protein coding sequence.

26. (previously presented) The herpes simplex virus of claim 19 wherein the marker comprises a defined nucleotide sequence detectable by hybridisation under high stringency conditions with a corresponding labelled nucleic acid probe.

27. (previously presented) The herpes simplex virus of claim 19 wherein the cassette further comprises nucleic acid encoding a polyadenylation sequence located downstream (3′) of the nucleic acid encoding the marker.

28. (previously presented) The herpes simplex virus as claimed in claim 27 wherein the polyadenylation sequence comprises the Simian Virus 40 (SV40) polyadenylation sequence.

29. – 32. (cancelled)

33. (previously presented) A method of lysing or killing tumour cells *in vitro* or *in vivo* comprising the step of administering to a patient in need of treatment the herpes simplex virus of claim 1.

34. (previously presented) A medicament, pharmaceutical composition or vaccine comprising the herpes simplex virus of claim 1.

35. (previously presented) The medicament, pharmaceutical composition or vaccine as claimed in claim 34 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

36. (currently amended) ~~An~~ The herpes simplex virus according to claim 1, ~~wherein the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO),~~ wherein (1) the nucleic acid sequence is in at least one of the long repeat regions (R_L), or (2) the herpes simplex virus is non-neurovirulent.

37. – 41. (cancelled)

42. (previously presented) A method for the treatment of a tumour comprising the step of administering to a patient in need of treatment the herpes simplex virus of claim 36.

43. (cancelled)

44. (previously presented) The method of claim 42 wherein said herpes simplex virus is capable of killing tumour cells.

45. (previously presented) A method of expressing in vitro or in vivo an antisense to the squamous cell carcinoma related oncogene (asSCCRO), said method comprising the step of infecting at least one cell or tissue of interest with the herpes simplex virus of claim 36, wherein asSCCRO is operably linked to a transcription regulatory sequence.

46. (cancelled)

47. (currently amended) The herpes simplex virus of claim 94, wherein the herpes simplex virus is HSV1716asSCCRO (ECACC accession number 04051901).

48. (currently amended) ~~An~~ The herpes simplex virus according to claim 94, wherein ~~the herpes simplex virus genome comprises~~ the nucleic acid ~~encoding~~ encodes a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide.

49. (previously presented) The herpes simplex virus according to claim 48 wherein said siRNA is capable of repressing or silencing expression of a mammalian SCCRO.

50. (previously presented) The herpes simplex virus according to claim 48 wherein said siRNA is capable of repressing or silencing expression of human SCCRO.

51. (previously presented) The herpes simplex virus according to claim 48 wherein said siRNA comprises a nucleic acid of between 10 and 70 nucleotides in length and having the sequence of SEQ ID No.5 or the complement thereof.

52. (previously presented) The herpes simplex virus according to claim 48 wherein said siRNA comprises a nucleic acid of between 10 and 70 nucleotides in length and having at least 70% identity to SEQ ID No.5 or the complement thereof.

53. (previously presented) The herpes simplex virus according to claim 52 wherein said degree of sequence identity is at least 80%.

54. (previously presented) The herpes simplex virus of claim 48 wherein said herpes simplex virus genome further comprises a regulatory sequence operably linked to said siRNA, wherein said regulatory sequence has a role in controlling transcription of said siRNA.

55. (previously presented) The herpes simplex virus of claim 48 wherein said nucleic acid is located in at least one RL1 locus of the herpes simplex virus genome.

56. (previously presented) The herpes simplex virus of claim 48 wherein the said nucleic acid is located in, or overlaps, at least one of the ICP34.5 protein coding sequences of the herpes simplex virus genome.

57. (previously presented) The herpes simplex virus of claim 48 wherein the herpes simplex virus is a mutant of one of HSV-1 strains 17 or F or HSV-2 strain HG52.

58. (previously presented) The herpes simplex virus of claim 48 wherein the herpes simplex virus is a mutant of HSV-1 strain 17 mutant 1716.

59. (previously presented) The herpes simplex virus of claim 48 which is a gene specific null mutant.

60. (previously presented) The herpes simplex virus of claim 48 which is an ICP34.5 null mutant.

61. (previously presented) The herpes simplex virus of claim 48 which lacks at least one expressible ICP34.5 gene.

62. (previously presented) The herpes simplex virus of claim 48 which lacks only one expressible ICP34.5 gene.

63. (previously presented) The herpes simplex virus of claim 48 which is non-neurovirulent.

64. (previously presented) The herpes simplex virus of claim 48 wherein said nucleic acid encoding said siRNA forms part of a nucleic acid cassette integrated in the genome of said herpes simplex virus, said cassette comprising nucleic acid encoding :

(a) said siRNA; and nucleic acid encoding:

(b) a first regulatory nucleotide sequence; and

(c) a marker,

wherein the nucleic acid encoding said siRNA is arranged upstream (5´) of the first regulatory nucleotide sequence and the first regulatory nucleotide sequence is arranged upstream (5´) of the marker, wherein said first regulatory sequence has a role in controlling transcription of said marker.

65. (previously presented) The herpes simplex virus according to claim 64 wherein a second regulatory nucleotide sequence is located upstream (5′) of the nucleic acid encoding said siRNA, wherein the second regulatory nucleotide sequence has a role in regulating transcription of said nucleic acid encoding said siRNA.

66. (previously presented) The herpes simplex virus as claimed in claim 64 wherein the cassette disrupts a protein coding sequence resulting in inactivation of the respective gene product.

67. (previously presented) The herpes simplex virus of claim 64 wherein the marker is a defined nucleotide sequence encoding a polypeptide.

68. (previously presented) The herpes simplex virus as claimed in claim 67 wherein the marker comprises the Green Fluorescent Protein (GFP) protein coding sequence or the enhanced Green Fluorescent Protein (EGFP) protein coding sequence.

69. (previously presented) The herpes simplex virus of claim 64 wherein the marker comprises a defined nucleotide sequence detectable by hybridisation under high stringency conditions with a corresponding labelled nucleic acid probe.

70. (previously presented) The herpes simplex virus of claim 64 wherein the cassette further comprises nucleic acid encoding a polyadenylation sequence located downstream (3´) of the nucleic acid encoding the marker.

71. (previously presented) The herpes simplex virus as claimed in claim 70 wherein the polyadenylation sequence comprises the Simian Virus 40 (SV40) polyadenylation sequence.

72. (previously presented) The herpes simplex virus of claim 48 for use in a method of medical treatment.

73. (previously presented) The herpes simplex virus of claim 48 for use in the treatment of cancer.

74. (previously presented) The herpes simplex virus of claim 48 for use in the oncolytic treatment of a tumour.

75. (cancelled)

76. (previously presented) A method of lysing or killing tumour cells *in vitro* or *in vivo* comprising the step of administering to a patient in need of treatment the herpes simplex virus of claim 48.

77. (previously presented) A medicament, pharmaceutical composition or vaccine comprising the herpes simplex virus of claim 48.

78. (previously presented) The medicament, pharmaceutical composition or vaccine as claimed in claim 77 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

79. (currently amended) ~~A~~ The herpes simplex virus according to claim 94, wherein the ~~genome of said virus comprises a~~ nucleic acid sequence ~~encoding~~ encodes a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide, and wherein (a) the siRNA is in at least one of the long repeat regions (R_L), or (b) the herpes simplex virus is non-neurovirulent.

80. – 85. (cancelled)

86. (currently amended) A method for the treatment of a tumour comprising the step of administering to a patient in need of treatment ~~a~~ the herpes simplex virus according to claim 79, ~~wherein the genome of said virus comprises a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide and wherein (a) nucleic acid sequence is in at least one of the long repeat regions (R_L), or (b) the herpes simplex virus is non-neurovirulent~~.

87. (previously presented) The method of claim 86 wherein said herpes simplex virus is capable of killing tumour cells.

88. (currently amended) A method of expressing in vitro or in vivo a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide, said method comprising the step of infecting at least one cell or tissue of interest with a herpes simplex virus according to claim 48, wherein the ~~genome of said virus comprises a~~ nucleic acid sequence encoding said siRNA in at least one of the long repeat regions (R_L), and wherein said nucleic acid sequence encoding said siRNA is operably linked to a transcription regulatory sequence.

89. (currently amended) A method of expressing in vitro or in vivo a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide, said method comprising the step of infecting at least one cell or tissue of interest with ~~a~~ the non-neurovirulent herpes simplex virus according to claim 63, wherein the ~~genome of said virus comprises a nucleic acid sequence encoding said siRNA, wherein said~~ nucleic acid sequence encoding said siRNA is operably linked to a transcription regulatory sequence.

90. (previously presented) A medicament, pharmaceutical composition or vaccine comprising the herpes simplex virus of claim 36.

91. (previously presented) The medicament, pharmaceutical composition or vaccine as claimed in claim 90 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

92. (previously presented) A medicament, pharmaceutical composition or vaccine comprising the herpes simplex virus of claim 79.

93. (previously presented) The medicament, pharmaceutical composition or vaccine as claimed in claim 92 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

94. (new) A herpes simplex virus wherein the herpes simplex virus genome comprises a nucleic acid capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide.